

DISSERTATION ON
PATTERNS OF DIFFUSE PARENCHYMAL LUNG DISEASE
MANIFESTATIONS IN COLLAGEN VASCULAR DISEASE
AND IN RELATION TO DLCO

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CERTIFICATE

This is to certify that the dissertation on “**PATTERNS OF DIFFUSE PARENCHYMAL LUNG DISEASE MANIFESTATIONS IN COLLAGEN VASCULAR DISEASE AND IN RELATION TO DLCO**” is a record of research work done by **DR.G.SANGAMITHRA** in partial fulfillment for M.D.BRANCH- XVII (T.B. AND RESPIRATORY DISEASES) EXAMINATION of The Tamilnadu Dr. M.G.R.Medical University to be held in March 2009. The period of study is from January 2008 to November 2008.

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DECLARATION

I hereby declare that the dissertation entitled “ **PATTERNS OF DIFFUSE PARENCHYMAL LUNG DISEASE MANIFESTATIONS IN COLLAGEN VASCULAR DISEASE AND IN RELATION TO DLCO** ” submitted for the Degree of Doctor of Medicine in M.D., DEGREE EXAMINATION Branch-XVII TUBERCULOSIS & RESPIRATORY DISEASES is my original work and the dissertation has not formed the basis for the award of any degree, diploma, associate ship, fellowship or similar other titles. It had not been submitted to any other university or Institution for the award of any degree or diploma.

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CONTENTS

		Page No
I	Introduction	1
II	Aim of the study	3
III	Review of Literature	4
IV	Materials and Methods	32
V	Results	37
VI	Discussion	50
VII	Conclusions	52
VIII	Abbreviation	
IX	Bibliography	
X	Master chart	
XI	Key to Master chart	

I. INTRODUCTION

Diffuse parenchymal lung diseases (DPLD) are a diverse group of pulmonary disorders that are classified together because of similar clinical, roentgenographic, physiologic, or pathologic manifestations¹. They are also referred to as interstitial lung diseases (ILD). DPLD alter mechanical and gas exchange properties of the lungs. In general, the hall marks of DPLD are restrictive changes in pulmonary physiology i.e decreased total lung capacity, reduced residual volume, diminished static compliance and reduced vital capacity often with an increased FEV₁/FVC ratio and a reduced diffusing capacity with carbon monoxide.

Hence pulmonary function testing (PFT) aids in the evaluation and management of patients with DPLD by provide an estimate of histologic severity, baseline estimation of prognosis and be used to monitor disease progression or response to therapy. The forced vital capacity and diffusion capacity are the most valuable serial measurements for diagnosing DPLD.

The collagen vascular diseases are a heterogeneous group of immunologically mediated inflammatory diseases. It is not surprising that, by virtue of their abundant connective tissue and blood supply, the lungs are frequently involved in these disorders. Consequently, collagen vascular diseases affect all areas of the lung (i.e. airways, alveoli, vascular system, and pleura), and do so in various degrees and combinations².

Diffuse parenchymal lung diseases in CVD patients are characterised by deteriorating parenchymal fibrosis and gas exchange. It remains innocuous in the early stage, as most of the rheumatic patients have restricted mobility manifesting with subtle or nil pulmonary symptoms. Hence, the respiratory physician should be prudent in

diagnosing the cases as early as possible. Because the pulmonary specialist often involved in care of these patients, a comprehensive understanding of collagen vascular disease and usual course of Diffuse parenchymal lung diseases are important.

The clinical assessment of a patient with DPLD requires a combination of history and physical examination, laboratory investigation, lung function testing, chest imaging studies, bronchoalveolar lavage, and histological examination.

Over the last few years, the abnormal patterns of DPLD on High Resolution Computerised Tomography (HRCT) scans have been refined and are increasingly recognised as diagnostic patterns. This has led to the increasing use of HRCT scans in conjunction with thorough clinical assessment³. By pulmonary function tests (PFT) the severity of physiologic disarrangements in DPLD, correlate well with the overall extent of pathologic and HRCT abnormalities⁴. Abnormalities of pulmonary function tests also verify the presence of disease particularly in those patients with normal chest roentgenograms.

This study throws light on the non-invasive procedures rather than the invasive procedures. Since most of the patients deny procedures like bronchoscopy or surgical biopsy as well as they are in real respiratory compromise, it is better to opt an alternate procedure like HRCT , Diffusing capacity for carbon monoxide (DLCO) and spirometry which are frequently done nowadays as an adjunct to aid the diagnosis.

II. AIM OF THE STUDY

To evaluate the Diffusing capacity for carbon monoxide among patients with Diffuse parenchymal lung disease in proven Rheumatologic illness showing various pattern of abnormalities in the High Resolution Computerised Tomography and correlate the same with spirometry.

DESIGN OF THE STUDY:

Prospective study.

Approval from Medical Ethical Committee has been obtained.

III. REVIEW OF LITERATURE

Diffuse parenchymal lung diseases (DPLD) commonly complicate the management of collagen vascular diseases. Hence a comprehensive understanding of collagen vascular disease and the usual cause of diffuse parenchymal lung disease is important. Approximately 15% of the patients who present with diffuse parenchymal lung diseases have an underlying collagen vascular disease⁵. Furthermore clinical symptoms like cough, dyspnoea or Diffuse Parenchymal Lung Disease may be the first manifestation of Rheumatic diseases. Finally it can result in significant morbidity and mortality.

The autoimmune mediated inflammation and fibrosis that characterises these diseases can easily and irreversibly disrupt the normal functioning of the lung. As a group they can affect each portion of the lung :- The pleura, alveoli, interstitium, vasculature, lymphatic tissue and of both small and larger airways. The lung diseases associated with collagen vascular disease may precede the clinical presentation of collagen vascular disease by five years or more⁵.

Full pulmonary function tests (PFT) should be performed in all cases of suspected DPLD with collagen vascular diseases. They aid in the diagnosis DPLD, assessment of disease severity, response to treatment, and prognosis. DLCO is typically reduced in DPLD to greater extent than the lung volumes at which it is measured. Co-existence of DPLD with obstructive airway disease (i.e.emphysema), can confuse the results with a mixed pattern of restriction observed as reduced lung volumes and obstruction manifesting as a reduced FEV1/FVC ratio.

Baseline PFT may provide an estimate of prognosis. Exertional oxygen desaturation to less than 88% and a decrease in FVC (greater than 10%) over a short follow up period predict patients at increased risk of mortality. Severely decreased DLCO (<30%) is also associated with increased mortality. Serial PFTs provide valuable information in determining disease progression and response to medication. FVC and DLCO are the most valuable serial measurements.

Many of these Collagen vascular diseases are characterised by the presence of the specific type of autoantibody that may greatly assist in specific diagnosis.

AUTO ANTIBODY ASSOCIATED WITH SPECIFIC COLLAGEN VASCULAR DISEASES⁷

Diseases	Associated Antibodies
Rheumatoid Arthritis	Rheumatoid factor
Systemic sclerosis	Antiscl-70
	Anticentromere Antibody
Mixed connective tissue diseases	Anti ribonuclear protein
Dermatomyositis/Polymyositis	Anti-Jo-1
Systemic lupus erythematosus	Anti-ds-DNA
	Anti-sm
Sjogren's syndrome	Anti ss-A(Ro)
	Anti ss-B(La)

The association of Collagen vascular disease and Diffuse parenchymal lung disease (DPLD) is well established⁶. DPLD complicating collagen vascular diseases account for high morbidity and mortality. Until recently, most of the studies of lung involvement in the collagen vascular disease relied on clinical, physiological and radiological data to define the presence of disease, determine the clinical course, and assess the prognosis of the lung involvement.

RHEUMATOID ARTHRITIS (RA)

It is a sub acute or chronic inflammatory polyarthropathy of unknown cause that particularly affects peripheral joints. Lung fibrosis associated with Rheumatoid arthritis was first reported by Ellman & Ball 1948⁸.

DPLD quickly appeared as the predominant pulmonary manifestation of rheumatoid arthritis (RA) (after excluding drug-induced pulmonary disease). Systematic PFTs detected a decreased diffusing capacity(DLCO) in 41% of patients, and among them, 50% exhibited features of fibrosis associated with lymphoid infiltrates in lung biopsy. Dawson and colleagues studied 29 patients with RA and found that DLCO < 54% of predicted had an 80% sensitivity and a 93% specificity for predicting progressive parenchymal lung disease over the next 2 years.

Prevalence of pleuropulmonary manifestations is clearly increased in males and in smokers. Coexisting subcutaneous rheumatoid nodules, high titres of circulating rheumatoid factor or antinuclear antibodies are also considered significant risk factors while the incidence of DPLD appears unrelated to the severity of articular disease.

Rheumatoid lung fibrosis is twice as common in men as in women with a mean age of about fifty years. RA is characterised by the presence of symmetric arthritis, morning stiffness and Rheumatoid factor in the blood.

Pleuropulmonary complications include interstitial pneumonitis with fibrosis, Rheumatoid (necrobiotic) nodules, Bronchiolitis Obliterans Organising Pneumonia, Bronchiectasis, Obliterative bronchiolitis, follicular bronchiolitis and pleural effusion or pleural thickening^{9,10}.

Interstitial pneumonitis with fibrosis are the most common pulmonary manifestations of Rheumatoid arthritis⁹. In fact pulmonary function abnormalities consistent with interstitial fibrosis have been reported in as many as 40% of patients who have Rheumatoid arthritis⁹. In more than half of these patients, however findings at chest roentgenogram are normal. Evidence of interstitial fibrosis is seen at chest roentgenogram in approximately 5%⁹ and at HRCT in 30% to 40%¹⁰ of patients with RA. The complication is seen most frequently in men between 50 and 60 years of age.

TYPES OF INTERSTITIAL PNEUMONIA

Non-specific interstitial pneumonia(NSIP), Usual interstitial pneumonia(UIP)

Cryptogenic organising pneumonia(COP) and

Lymphocytic interstitial pneumonia(LIP).

The majority of the patients with interstitial fibrosis associated with RA have UIP, and only a small percentage have histological findings of NSIP. Nodular aggregates of

lymphocytes may be prominent in both the parenchymal interstitium and in the interstitial tissue in bronchiolar walls and interlobular septa(Follicular bronchiolitis).

RADIOLOGIC MANIFESTATIONS

Initial radiographic studies found a low incidence of 1.6–5% of DPLD in RA⁸. In the early stage, the radiographic appearance consists of irregular linear hyper attenuating areas in a fine reticular pattern. The abnormality usually involves mainly the lower lung zones. With the progression of disease, the reticular pattern becomes coarser and diffuse and later honeycombing may be seen¹¹.

HRCT FINDINGS

HRCT findings consist of irregular linear hyper attenuating areas caused by a combination of intralobular lines and irregular thickening of interlobular septa¹⁰. Honeycombing is seen more markedly near the diaphragm. HRCT demonstrates interstitial lung disease in patients with or without clinical evidence of the disease (69%–80% and 20%–29% respectively)¹⁰.

In a study by Akira et al, three major radiographic patterns of disease have been identified in symptomatic patients who developed lung disease prior to or following the diagnosis of RA¹². These include reticulation with or without honeycombing (66% patients), centrilobular branching lines with or without bronchial dilatation (17%), and consolidation (17%).

SPIROMETRY IN RA

The physiologic abnormalities of rheumatoid DPLD are identical to the other fibrosing lung diseases¹³. There is a reduction in pulmonary compliance and lung volumes. Physiologic testing also often shows evidence of obstruction to airflow, which may reflect other pulmonary manifestations of RA including bronchiectasis, bronchiolitis obliterans, chronic airway obstruction or cricoarytenoid arthritis^{14,15}.

DLCO IN RA

Abnormalities of gas transfer including a low DLCO is present in RA. Abnormal pulmonary function may be found in individuals with normal chest roentgenograms¹⁴.

SYSTEMIC SCLEROSIS (SS)

It is a generalised collagen vascular disease characterised by the synthesis and deposition of excessive extracellular matrix and vascular obliteration in various organs¹⁶.

Dr. Charlie Strange from the Medical University of South Carolina provided an algorithm for the management of DPLD in scleroderma patients that includes chest x-rays, spirometry, and DLCO. If the results are normal, these tests should be repeated on a 6-month basis. If any of the findings are abnormal, an HRCT should be obtained. All patients with scleroderma undergo annual echocardiography and measurements of their DLCO. A DLCO < 40% of predicted appears to be predictive for underlying Pulmonary Arterial Hypertension(PAH), and an FVC/DLCO ratio >1.8 has good performance characteristics in PAH.

SS is divided into two broad categories: Diffuse and limited forms based on the extent of cutaneous involvement, different clinical course and prognosis.

Most common clinical manifestations are

Tightening, induration and thickening of the skin (SCLERODERMA),

Raynaud's and other vascular anomalies,

Musculoskeletal manifestation and

Visceral involvement particularly Gastro Intestinal Tract, Lungs, Heart and Kidney.

The diagnosis can be made with a high degree of certainty if the single major criterion of proximal scleroderma is present or if there are 2 or more minor criteria (sclerodactyly, pitting scars or loss of the substance of fingertips and bilateral basal pulmonary fibrosis)⁸. Systemic Sclerosis has 3:1 female to male distribution and presents more commonly in the third to fifth decade of life.

Lung is the fourth most commonly affected structure after skin, vessel and oesophageal involvement⁷. Pulmonary involvement is more common and more severe in systemic sclerosis than in other types of collagen vascular disease. Prognostic factors for poor outcomes include male sex, the presence of lung involvement early in disease, low DLCO, severe Raynaud's phenomenon, and cigarette smoking.

RADIOLOGIC MANIFESTATIONS

Pulmonary fibrosis is the most common radiographic finding, present in 20% –65% of patients^{16, 17}. The fibrosis usually has a basilar predominance and appears initially as a fine reticular pattern that progresses to coarse reticulation and honeycombing¹⁶. Pulmonary fibrosis is equally likely in the limited and diffuse forms of

the disease but is less severe in the limited form. In Schurawitzki H, Stiglbauer R, Graninger W, et al prospective study of 23 patients with systemic sclerosis, fibrosis was identified at chest radiography in 39% of patients and at high-resolution CT in 91% of patients ¹⁷.

HRCT FINDINGS

The predominant abnormalities at high-resolution CT consist of areas of ground-glass attenuation, poorly defined sub pleural nodules, reticular pattern of attenuation, honeycombing, and traction bronchiectasis ¹⁷.

In Kim et al¹⁸ longitudinal CT series of 40 patients with SS study , a variety of radiological features were found including ground-glass opacity (100%), irregular linear opacity (90%), small nodules (70%), honeycombing (33%), traction bronchiectasis (68%), bilateral pleural thickening (45%), and enlarged mediastinal lymph nodes (15%). After a mean follow-up of 40 months, regardless of the initial findings or presence of treatment, the extent of parenchymal disease, including ground-glass opacity and honeycombing, significantly increased with concomitant declines in forced expiratory volume in 1 second (FEV₁), and forced vital capacity (FVC) without significant change in DLCO¹⁸.

SPIROMETRY IN SS

Physiological studies have shown a restrictive pattern with a decreased total lung capacity (TLC), vital capacity (VC), forced vital capacity (FVC) and residual volume. The greatest decline in lung function occurs within the first 4 years of disease and moderate (forced vital capacity [FVC] 50-75% predicted) or severe (FVC< 50%

predicted) restrictive lung disease is detectable in approximately 40% of patients with scleroderma. Initially, there may be a reduction in DLCO, which may even precede symptoms onset and/or loss of lung volume. Occult pulmonary impairment may be present in patients with normal pulmonary function tests (PFT) which may be demonstrated by cardio-respiratory exercise testing ¹⁹.

DLCO IN SS

In SS impairment of the transfer factor (or diffusing capacity) for carbon monoxide (DLCO) is present. A reduced DLCO is the most common and most sensitive PFT abnormality in patients with scleroderma and has been shown to correlate with the presence of dyspnoea and with autopsy, evidence of DPLD. With progression of the DPLD, the restrictive pattern is paralleled by the decrease in gas exchange. As demonstrated by WELLS et al.²⁰, DLCO is the best index of the extent of the DPLD when compared with HRCT as the "gold standard". Interestingly, patients with DPLD-scleroderma have a better survival rate (86% at 5 yrs) than patients with idiopathic pulmonary fibrosis (IPF) (50% at 5 yrs)²¹.

Reduced DLCO in SS

1. Related to alveolar septal thickening and vascular obliteration
2. May be the earliest PFT abnormality and the most sensitive indicator of SS ²²
3. Degree of decline corresponds to the severity of dyspnoea
4. Severe isolated reduction in DLCO (<45% of the predicted value) is an early indicator of Pulmonary arterial Hypertension²³.

A low DLCO is more common in limited form than in diffuse form. FVC and DLCO are important prognostic factors in scleroderma²⁴.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

The original description of SLE is credited to Kaposi in 1872.²⁵ It is a multisystem disorder that particularly affects vessel, serosa, kidneys, central nervous system, skin, blood vessels, joints and lung. SLE is characterised by the presence of auto antibodies against various nuclear antigens. It predominantly affects women (F:M ratio 10:1) aged 20–50 years.

During the course of SLE, pleural disease develops in 50% of patients²⁶. Pulmonary parenchymal abnormalities are also common. Pleuropulmonary involvement occurs in approximately 50%–60% of patients. In one prospective study that included 1,000 patients, lung involvement was identified in only 3% at the onset of the disease; it developed in an additional 7% of patients over the period of observation. Parenchymal opacification may be caused by pneumonia, haemorrhage, acute lupus pneumonitis, or pulmonary oedema, with pneumonia being the most common cause²⁶.

Pulmonary manifestations of systemic lupus erythematosus comprise both acute and chronic lesions. Acute disease includes pulmonary haemorrhage, acute lupus pneumonitis and pulmonary oedema. Chronic disease such as interstitial pneumonitis with fibrosis is less common than in other connective tissue disorders²⁷.

Most frequent lung manifestation in SLE results from acute injury to the alveolar-capillary unit, leading to acute lupus pneumonitis and/or alveolar haemorrhage^{28,29}. Acute lupus pneumonitis is an abrupt febrile pneumonic process

without infectious aetiology. The alveolar haemorrhage varies from mild to massive, and BAL studies often reveal haemosiderin-laden macrophages. It presents with dyspnoea, tachycardia, cough, fever, pleuritic chest pain and sometimes haemoptysis.

ACUTE LUPUS PNEUMONITIS

Acute lupus pneumonitis is characterized by the acute or sub acute onset of tachycardia, tachypnea, dyspnoea, cyanosis, and cough. Fever is common, but haemoptysis is infrequent, and clubbing is absent. The mean age in one series was 38 years with a mean duration of known SLE of 16 months (range 0 to 48 months). In 50% of these patients, pneumonitis was the presenting manifestation of their SLE. Chest examination may reveal fine or coarse rales, but signs of pleurisy are rare. In severe cases, evidence of right ventricular overload may appear.

The chest radiograph plays a limited role in the differential diagnosis of pulmonary complications of SLE. The most common findings in patients with SLE are non-specific areas of air space consolidation. The consolidation may be unilateral or bilateral and focal or diffuse, but it tends to involve mainly the lower lung zones. The most common cause of consolidation is pneumonia

Chest roentgenograms in the acute lupus syndrome demonstrate diffuse or patchy opacities that are predominantly basilar, although the middle and upper zones may be affected. Usually bilateral, the opacities may be accompanied by pleural effusion and cardiomegaly. A recent case report described acute lupus pneumonitis in a patient with a normal chest radiograph and HRCT scan. Sub acute cases may demonstrate the migratory, recurrent, and polymorphic densities. Marked hypoxemia and hyperventilation

are often described in acute pneumonitis. Such deficits in particular cause an elevation of the alveolar-arterial gradient; persist in the majority (of a small number) of patients despite the apparent resolution of their lung disease.

RADIOLOGIC MANIFESTATIONS

The most common radiographic manifestation is unilateral or bilateral pleural effusion that is frequently associated with pericardial effusion³⁰. Chest radiographs typically show unilateral or bilateral patchy areas of consolidation, mostly predominant in the lung bases, which may be associated with pleural effusion or atelectasis. Other chest radiographic findings of SLE include loss of lung volume related to diaphragmatic dysfunction, pulmonary oedema, musculoskeletal changes related to renal failure, and bone changes related to corticosteroid therapy.

HRCT FINDINGS

Multiple patterns have been reported in SLE. The most common findings are intralobular interstitial thickening and irregular thickening of the interlobular septa that are predominantly found in the lower lobes^{31,32}. Other common findings on HRCT include traction bronchiectasis (architectural distortion and bronchial dilatation secondary to the fibrosis), small foci of air space consolidation, and areas of ground-glass attenuation^{31,32}. Honeycombing changes may be present. Both pleural effusions and cardiomegaly may be noted. Enlargement of the pulmonary artery accompanies cor pulmonale.

SPIROMETRY & DLCO IN SLE

Several studies indicate that physiologic abnormalities (e.g., DLCO, lung volumes, or compliance) are more common than clinical or roentgenographic changes³³. Most common physiologic deficit in patients with SLE is the reduction in DLCO with or without decreased total lung capacity. Among patients with normal chest roentgenograms, a reduction in VC was noted in 27% and in DLCO in 67%³⁴. In two series of unselected patients, a reduction in DLCO occurred more frequently (72 to 80%) than did volume restriction (43 to 49%) or roentgenographic abnormalities (30 to 50%)³⁵.

POLYMYOSITIS/DERMATOMYOSITIS (PM/DM)

Polymyositis is an autoimmune inflammatory myopathy characterised by presence of symmetric weakness of the limb girdle and anterior neck muscles³⁶. Dermatomyositis is similar to polymyositis except for the presence of a characteristic skin rash. PM/DM have an incidence of approximately 5–10 cases per million per year³⁶ and occur twice as often in women as in men. The diagnostic criteria for PM/DM are proximal muscle weakness (Symmetric, present for weeks or months), Muscle biopsy showing necrotic and inflammatory changes, Raised muscle enzymes (Creatine phosphokinase), Characteristic electromyography and Characteristic skin rash. In Dermatomyositis additional characteristic skin changes present: Heliotrope periorbital rash and violaceous/red papular rash over bony prominence.

PM/DM is often associated with clinical, radiological or functional evidence of pulmonary fibrosis. Mills and Mathews first described interstitial fibrosis in Dermatomyositis in 1956. In two retrospective studies, DPLD were found in 5% of PM

and 9% of DM cases³. Lung involvement in PM/DM may precede muscle or skin manifestations in 33% of cases. There is no correlation between the extent and severity of muscle and skin involvement and the development of DPLD.

The clinical presentation may be arbitrarily divided into three forms.

- 1) DPLD may occasionally be rapidly progressive with acute fever, dyspnoea and lung infiltrates similar to a Hamman-Rich-syndrome.
- 2) Patients may have a slowly progressive dyspnoea upon exertion with chest radiographic abnormalities.
- 3) Some patients may have no pulmonary symptoms, but abnormal radiographs and/or PFT.

RADIOLOGIC MANIFESTATIONS

Chest radiographs most often reveal bilateral basal infiltrates, but may be normal in patients with biopsy proven DPLD. HRCT shows pleural irregularities, ground glass attenuation and patchy consolidation³⁸. The frequency of radiographic parenchymal abnormalities is low (about 5%). The most common is a symmetric, predominantly basal reticular pattern that may become diffuse over time and progress to honeycombing³⁶. Bilateral areas of consolidation develop in some patients over a 2- to 3-week period.

HRCT FINDINGS

The HRCT findings are prominent interlobular septa, ground-glass attenuation, patchy consolidation, parenchymal bands, irregular peribronchovascular thickening, and sub pleural lines. Honeycombing may be seen in up to 16% of patients who have

abnormal chest radiographic findings or pulmonary function tests³⁹. Patchy consolidation, parenchymal bands, and irregular peribronchovascular thickening are seen to improve at sequential CT, becoming pleural irregularities, prominent interlobular septa, ground-glass attenuation, and sub pleural lines on follow-up CT scans. Therefore, consolidation with patchy and sub pleural distribution, parenchymal bands, and irregular peribronchovascular thickening are reversible. On occasion, areas of ground-glass attenuation with parenchymal bands or sub pleural lines that represent a pathologic area of usual interstitial pneumonia may progress to honeycombing.

SPIROMETRY & DLCO IN PM/DM

These patients usually have evidence of a restrictive ventilatory pattern with reductions in VC and TLC. In addition, the DLCO may also be reduced. The profound respiratory muscle weakness, which may often complicate these patient's courses, may be demonstrated by a decrease in maximal inspiratory pressure, maximal inspiratory flow rate and maximal voluntary ventilation. Many patients have resting arterial hypoxemia, which is made worse with exercise. Clinical exercise testing is of importance in PM/DM patients to elucidate the cause of dyspnoea, which may not be limited to DPLD, but might be due in part to pulmonary hypertension, cardiac dysfunction or muscle weakness⁴⁰.

SJOGREN'S SYNDROME

Sjogren's syndrome, or the sicca complex, is an autoimmune exocrinopathy characterized by lymphocytic infiltration of glandular and extra glandular organs. A clinical triad of dry eyes (keratoconjunctivitis sicca), dry mouth (xerostomia), and

arthritis characterizes Sjogren's syndrome. It is relatively common, affecting 0.1% of the general population and 3% of older adults⁴¹. It may be primary without features of other collagen vascular disease, or secondary in association with other collagen vascular disease most often rheumatoid arthritis.

Pulmonary manifestations occur frequently in Sjogren's syndrome. Diffuse parenchymal lung disease is probably the most common functional abnormality identified in patients with primary Sjogren's syndrome with lung involvement. The aetiology of DPLD associated with Sjogren's syndrome is unknown, and it appears that lymphocytic pneumonitis represents only one pole of the spectrum of diseases, which includes pseudo lymphomas and malignant lymphomas. DPLD occur more often in patients with extra glandular manifestations than in those with glandular disease alone.

The most common thoracic complication, lymphocytic interstitial pneumonia is followed in frequency by airway abnormalities such as follicular bronchitis, bronchiectasis, and bronchiolitis. Less common complications include interstitial pneumonitis and fibrosis, BOOP, lymphoma, pulmonary hypertension, and pleural effusion or fibrosis. A large series of 343 patients reported by STRIMLAN⁴² clearly demonstrated that many patients do not manifest as a single type of pulmonary lesion.

RADIOLOGIC MANIFESTATIONS

Parenchymal abnormalities are evident at chest radiography in 10%–30% of patients. The most common finding, a reticulonodular pattern that involves mainly the lower lung zones, may reflect the presence of lymphocytic interstitial pneumonia or interstitial fibrosis. In patients with interstitial opacities on their chest radiograph, a

restrictive pattern with a low diffusion capacity is commonly found on lung function tests.

HRCT FINDINGS

In Franquet et al study of high-resolution CT findings among 50 patients with Sjogren's syndrome showed the major abnormalities of bronchiectasis, bronchiolar inflammation and increased parenchymal line⁴³. There is an increased prevalence of lymphocytic interstitial pneumonitis that is seen radiographically as a reticulonodular pattern predominantly involving the lower lobes.

A recent article described the high-resolution CT findings of lymphocytic interstitial pneumonia⁴⁴, with the most common findings being areas of ground glass attenuation, thickening of bronchovascular bundles with interlobular septa and cysts. DPLD and bronchiolar inflammatory changes are common abnormal findings seen on HRCT scans in primary Sjogren's syndrome. For example, 20% of patients with primary Sjogren's syndrome undergoing HRCT had bronchial wall thickening with either ground-glass opacification or a small nodular pattern in the majority of these cases.

SPIROMETRY & DLCO IN SJOGREN'S SYNDROME

Bariffi and colleagues studied 18 female non-smokers with Sjogren's syndrome. They found that 13 of the 18 had an FEV₁/FVC ratio of less than 80% and 7 of 18 had an FEV₁ of less than 80%, whereas 9 of 14 had a maximum flow at 25% of VC (MEF25) of less than 80%⁴⁵. In addition, these investigators found abnormalities in diffusing capacity. Constantopoulos and colleagues, in a study of 61 patients with primary Sjogren's syndrome, at least 50% of patients had a decline in either MEF25 or MEF50,

whereas only 10% had a low FEV₁⁴⁶. However, other investigators performed a longitudinal study of 18 asymptomatic, non-smoking women with normal chest radiographs. In this group, baseline FEV₁/FVC, FVC, and TLC were normal in all patients. Only 17% had a diffusion defect.

When compared with secondary Sjogren's syndrome, there was a higher incidence of restrictive pattern in primary Sjogren's syndrome whereas an obstructive ventilator defect was more common in secondary Sjogren's syndrome or RA alone. The significance of diffusion defects in patients with primary Sjogren's syndrome remains of uncertain significance; in a 10-year follow-up of pulmonary involvement in 30 patients, a significant decline in diffusion was seen at 4 years followed by a significant improvement at 10 years, in the absence of any intervention.

MIXED CONNECTIVE TISSUE DISEASE (MCTD)

The term mixed connective tissue disease refers to a condition in which patients have mixed features of systemic lupus erythematosus, progressive systemic sclerosis, and polymyositis. There is an 8:1 female to male ratio and no racial predilection. Suggested clinical criteria for the diagnosis are 1) Positive for anti RNP plus 2) Three or more clinical features such as Hand oedema, Synovitis, Myositis, Raynaud's phenomenon and Acrosclerosis. After several years, MCTD may transform into one of the classic disease.

Pulmonary involvement has been described in 20–85% of patients with mixed connective tissue disease (MCTD)⁴⁷. Common pulmonary abnormalities include interstitial pneumonitis with fibrosis, pulmonary hypertension and pleural effusion. Clinical features of DPLD associated with MCTD are similar to those reported in

scleroderma and consist of Idiopathic Pulmonary Fibrosis with alveolar inflammatory processes and progressive development of honeycomb formation; generally, the degree of fibrosis appeared more severe in patients exhibiting scleroderma feature.

Radiologic manifestations

One-third of patients with mixed connective tissue disease had initial chest roentgenograms that were abnormal demonstrating small irregular opacities involving the lung base.

HRCT FINDINGS

In HRCT Pulmonary involvement in mixed connective tissue disease has been characterized as the presence of ground-glass attenuation, nonseptal linear opacities, with a peripheral and lower-lobe predominance. The frequency of pulmonary abnormalities varies considerably in different series. In a review of the CT findings in 41 patients with MCTD, Kozuka et al found ground glass, sub pleural micro nodules, non-septal linear and reticular abnormality in more than 50% of cases.

In a retrospective study of 81 patients at the Mayo Clinic⁴⁸, an interstitial pattern was seen at chest radiography in 19%; on the other hand, careful prospective study of 34 patients in another investigation showed interstitial abnormalities in 85%. The abnormalities consist of irregular linear hyper attenuating areas with a reticular pattern and involving mainly the lung bases. With the progression of disease, the fibrosis gradually extends superiorly; in the late stage, honeycombing may be identified. High resolution CT shows a predominant sub pleural distribution of fibrosis. Other radiological

abnormalities include areas of parenchymal consolidation that may be related to Bronchiolitis Obliterans Organising Pneumonia.

SPIROMETRY & DLCO IN MCTD

Pulmonary function abnormalities include a reduction of the DLCO, a decreased VC, TLC, and FEV₁. Abnormal PFT and chest radiographs are frequent. Impaired DLCO has been reported in 67%, and restrictive lung volumes in 50% of MCTD. DLCO appears to be the most sensitive single parameter in evaluating pulmonary dysfunction in MCTD.

RADIOLOGIC IMAGING IN DPLD

Patients with suspected DPLD will have a chest radiograph as the initial imaging investigation. In most cases, this is abnormal and occasionally the radiographic appearances are sufficiently characteristic to enable a specific diagnosis to be made when taken in conjunction with the clinical and laboratory findings. Chest radiograph is an essential test for the assessment of DPLD, however a normal Chest Radiograph cannot exclude the diagnosis. If available, previous x-rays or reports of x-rays should be obtained and compared with the recent x-rays. In appropriate clinical settings, HRCT may be sufficiently characteristic to preclude the need for biopsy⁷.

PULMONARY HRCT

HRCT scanning is capable of imaging the lung with excellent spatial resolution and providing anatomical detail similar to that seen by gross pathological examination. Images are usually obtained in the supine and prone position. In normal patients, dependent lung opacity is often seen in the posterior, subpleural regions of the lung. In certain diffuse lung diseases, such as nonspecific interstitial pneumonia (NSIP), images

can be identical to those seen in normal patients. Prone images will differentiate between these two possibilities, since normal dependent density in the posterior lung will disappear on prone images, whereas true lung disease-related density will persist. Dynamic expiratory images are also obtained to screen for air trapping.

1.Detection of DPLD

HRCT scanning is able to detect DPLD not visible on the chest radiograph. The relative sensitivities of the two techniques for the detection of DPLD are 94% and 80%, respectively.

2.Characterisation of disease and extent of disease

The diagnostic accuracy of HRCT scanning is further increased by concurrent clinical evaluation⁴⁹.Unlike chest radiography, HRCT scans provide cross sectional images and the extent of disease is therefore much more readily appreciated than on the chest radiograph. HRCT scanning may also elucidate patients with complex lung function abnormalities—for example, co-existing fibrosing alveolitis and emphysema.

3.Impact on lung biopsy samples

HRCT scanning has a high degree of accuracy in many forms of DPLD. The percentage of first choice diagnoses made with a high level of confidence in two studies was 82% and 93%.Fibrosing alveolitis may be confidently distinguished from other forms of DPLD with an accuracy of 88%. Using Bayesian analysis, Grenier *et al* concluded that the combination of clinical, radiographic, and HRCT findings enabled a

correct diagnosis with a high level of confidence in 61–80% of patients with DPLD.

Based on the findings it is evident that HRCT scanning can prevent the need for a histological diagnosis. For patients in whom lung biopsy samples are required, HRCT scanning is better able to differentiate between the need for transbronchial biopsy or open lung biopsy samples. It is also able to determine the most appropriate areas from which the biopsy samples should be taken.

4.Assessment of disease activity

There is evidence that a predominant ground glass pattern and is more likely to represent active inflammatory disease and to respond to appropriate therapy Reticular and honeycomb patterns on HRCT scans correlate well with histological evidence of fibrosis.

5.Prediction of response to treatment

Because of its ability to differentiate between cellular and fibrotic disease with reasonable accuracy, HRCT scanning can be used to predict response to treatment and is significantly more accurate than chest radiography in this respect.

HRCT PATTERNS⁵⁰

1. Reticular opacities: Thickening of the interstitial connective tissue network of the lung will result in reticular opacities of varying morphology. This thickening can result from fluid/cellular infiltration or deposition of fibrous tissue.

2. Nodules: There are several ways to classify nodules: well defined vs. poorly defined; upper vs. lower lobe distribution; and relationship to the secondary pulmonary lobule. The last is the most useful characteristic, since it provides a focused differential diagnosis and is reflective of the underlying disease pathophysiology. There are three possible HRCT distributions of nodules: perilymphatic, random, and centrilobular.

3. Honeycombing: Honeycomb lung remodelling (honeycombing) reflects the end stage of a number of diseases that cause parenchymal destruction. It presents a characteristic HRCT pattern, with subpleural, thick-walled cysts that share walls and, when advanced, are often stacked in multiple layers. Other signs of fibrosis (traction bronchiectasis and reticulation) typically accompany it. Honeycombing is highly suggestive of a pathologic diagnosis of usual interstitial pneumonia (UIP), although it can be attributable to other diseases

4. Traction bronchiectasis: Bronchial dilatation occurring as a consequence of interstitial fibrosis is referred to as traction bronchiectasis. The bronchi often appear irregular (corkscrewed) and are not associated with radiologic evidence of bronchial inflammation (gross bronchial wall thickening or mucous impaction). Other signs of lung fibrosis (honeycombing or irregular reticulation) often accompany traction bronchiectasis. While traction bronchiectasis is quite specific for fibrosis, the differential diagnosis is broader than that of honeycombing. In patients with known collagen vascular disease, bibasilar, peripheral, traction bronchiectasis accompanied by ground-glass attenuation can be considered diagnostic of NSIP.

5. Ground glass opacity:GGO is increased lung opacity that does not obscure the associated vessels and represents abnormalities below the resolution of HRCT. GGO has been associated with active or reversible lung disease. However, ground-glass opacity can also be seen in cases in which fibrosis is the predominant abnormality. Ground-glass attenuation can only be considered as reflecting the presence of potentially reversible disease if there are no associated findings of fibrosis in the same area. The differential diagnosis of ground glass opacity should be based upon the host immune status and duration of symptoms. The presence of connective tissue diseases, environmental inhalants, and drug use also should be considered when increased diffuse lung opacity is present.

Pulmonary Function Tests

Full pulmonary function tests (PFT) should be performed in all cases of suspected DPLD. They aid in the diagnosis, assessment of disease severity, response to treatment and prognosis. PFT measurements should include forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, vital capacity (VC) and diffusion capacity of carbon monoxide (DLCO).

Lung function tests are usually restrictive with small lung volumes seen as reduced VC in DPLD. The FEV_1/FVC ratio is either maintained or often increased. DLCO is typically reduced in DPLD to greater extent than the lung volumes. Coexistence of DPLD with obstructive airway disease (e.g. emphysema), can confuse the results with a mixed pattern of restriction observed as reduced lung volumes and obstruction manifesting as a reduced FEV_1/FVC ratio. DPLD are usually thought to be characterised

by restrictive lung function, by which is meant a reduction in lung volumes with preserved ratio of forced expiratory volume in one second.

Diagnosis and assessment of diffuse parenchymal lung disease can be done with FEV₁, forced vital capacity (FVC), FEV₁/FVC ratio, and VC together with a reduction in carbon monoxide transfer factor (DLCO). However, in early disease lung volumes and transfer factor may be within the normal range. In systemic sclerosis, an isolated reduction in DLCO may point to pulmonary vascular disease. In one study, 19% of PSS patients had such abnormal lung function, 11% of whom developed isolated pulmonary hypertension and the risk increasing markedly with lower DLCO. Patients may often be too ill to perform the tests and the investigations lack the appropriate sensitivity and specificity to be of diagnostic value.

Lung function tests are conventionally used to give a global index of functional impairment. Vital capacity (VC), total lung capacity (TLC), and DLCO are most commonly used while in the UK, exercise testing is used relatively little. Several studies have correlated lung function and exercise test parameters with the degree of pathological abnormality on lung biopsy samples using the latter as the gold standard. Watters et al developed a composite clinical radiographic physiological (CRP) score using seven variables: dyspnoea, chest radiograph, FEV₁ and FVC, TLC, DLCO/VA, resting A-a gradient, and exercise oxygen saturation.

ATS RECOMMENDATION FOR PERFORMING DLCO⁵¹

Equipment

1. Volume accuracy same as for spirometry($\pm 3\%$ over 8L range, all gases)
2. Documented analyzer linearity from 0 to full span $\pm 1\%$
3. Circuit resistance less than 1.5cm H₂O at 6 L/sec flow
4. Demand valve sensitivity less than 10 cm H₂O to generate 6L/sec flow
5. Timing mechanism accurate to $\pm 1\%$ over 10 sec; checked quarterly
6. Documented instrument dead space(Inspiratory/Expiratory) less than 0.1L
7. Check for leaks and volume accuracy(3L calibration) daily
8. Validate system by testing healthy non smokers (Biologic control) quarterly

Technique

1. Subject should refrain from smoking for 24 hours before the test
2. Subject should be instructed carefully before the procedure
3. Subject should inspire rapidly;2.5 sec or less for healthy subjects, 4 sec or less in obstruction
4. Subject should achieve an inspired volume greater than 90% of VC
5. Subject should achieve breath hold for 9-11 sec, relaxing against closed glottis or closed valve (No valsalva or mullers manoeuvre)

6. V_D wash out should be 0.75 L-1.0L(0.5 L if VC less than 2.0 L)
7. Alveolar sample volume should be 0.5-1.0 L collected in less than 4 sec
8. Visual inspection of V_D washout and alveolar sampling should be used for system that continuously analyzes expired gas
9. Test gas should contain 21% O_2 at sea level; supplemented O_2 should be discontinued before testing if possible
10. Four minutes should elapse between repeat tests

Calculations

1. Average at least two acceptable tests; duplicate determinations should be within 10% or 3ml/min/mm of Hg
2. Use Jones method of timing of breath hold
3. Alveolar volume should be determined by single breath dilution of tracer gas
4. Adjust for V_D volumes (Instrument and patient)
5. Determine inspired gas conditions(ATPS or ATPD)
6. Correct for CO_2 and H_2O absorption
7. Report D_L/V_A in ml CO (STPD)/min/mm Hg per L(BTPS)
8. Correct for Haemoglobin concentration
9. Adjust for COHb

10. Adjust for altitude

11. Use reference equations appropriate to the laboratory method and patient population

Acceptable test criteria for diffusing capacity of the lung for carbon monoxide

Use of proper quality-controlled equipment,

V_I (Inspired Volume) of $>85\%$ of largest VC in <4 sec,

A stable calculated breath hold for 10 ± 2 s. There should be no evidence of leaks, or

Valsalva or Mueller maneuvers,

Expiration in <4 s (and sample collection time <3 s), with appropriate clearance of V_D

(Dead space volume) and proper sampling/analysis of alveolar gas.

Pulmonary Function Tests in DPLD⁵²

1. Severity and pattern of disease

Simple lung function testing using lung volumes and gas transfer factor gives a reasonable measure of the extent of disease.

2. Monitoring the course of the disease

VC and DLCO are the most appropriate and simplest indicators of change in DPLD. DLCO predict survival in some studies. In Wells et al²⁰ study, increased mortality is associated with reduced DLCO, FVC and TLC. The one index that appears to be a good predictor of the subsequent clinical course is DLCO.

IV. MATERIALS AND METHODS

This prospective study was organized in the Institute of Thoracic medicine and department of Thoracic medicine, Government General Hospital in association with department of Rheumatology, Government General Hospital. Subjects were recruited from the Pulmonary and Rheumatology outpatient clinic of our hospital. This study was approved by the ethical committee of this institution.

The design of the work is a prospective study. The study extended from the period of January 2008 to November 2008 and it was performed at the Institute of Thoracic medicine with the same population referred from the department of Rheumatology, Government General Hospital, Chennai.

INCLUSION CRITERIA

1. Clinically and radiologically confirmed cases of DPLD.
2. Age > 12 years.
3. Sex- Both genders.
4. Patients who are able to perform spirometry and diffusion capacity with a breath holding period of at least 10 seconds.
5. Serologically positive collagen vascular disease patients.

EXCLUSION CRITERIA

1. Patient associated with history suggestive of Infection, Allergy and immunosuppression.

2. Patient associated with any other respiratory disease, cardiovascular disease, and malignancy.
3. Smokers are virtually eliminated from the study as a confounding factor (For example respiratory bronchiolitis of smoking can be falsely attributed to collagen vascular disease).
4. DPLD due to other causes or of unknown aetiology.
5. Breath-holding time <9 or >11 seconds, or with an inspiratory capacity less than 85% of the largest previously measured vital capacity.

METHODOLOGY

In essence, without proper medical history all Diffuse parenchymal lung diseases are of unknown cause. For an accurate diagnosis, there is no substitute for complete clinical evaluation. This should be considered as the key diagnostic steps in the evaluation of patient who has DPLD.

Thorough history elicitation with comprehensive evaluation of the chief complaint and comprehensive review of multiple systems were done.

Medical history was taken with special reference to previous cardiopulmonary disease, cough, exertional dyspnoea, sputum, chest pain and risk factors for pulmonary disease, such as smoking.

Then followed by exhaustive review of past medical, social, family and occupational histories with an exploration of all potential environmental exposures were

done. The clues that surface during this evaluation help to narrow the broad differential diagnosis to few possible disorders as per ATS recommendation.

PULMONARY HRCT

The patients were then subjected to the High-resolution computed tomography (HRCT) in the supine position, holding breath at deep inspiration, without contrast medium. Prone sections were taken when posterior images obtained on supine sections were suspected of having artefacts due to gravity dependent perfusion. The added value of HRCT scanning in DPLD depends upon its ability to increase confidence of a specific diagnosis by characterisation and profusion of lesion on representative anatomical level, to alter patient management and if possible, to influence the outcome⁴⁹. (Fig A, B, C &D).

Pulmonary Function Tests

After completing the physical examination and HRCT of those who have fulfilled criteria, were subjected to pulmonary function test. The various manoeuvres of PFT were explained and practically demonstrated to them.

PFT was deferred to those persons who were suspected of having respiratory tract infection. A course of antibiotics were given to them and asked to come for the next session for the completion of PFT.

ATS RECOMMENDATION FOR PERFORMING SPIROMETRY⁵¹

Procedures for recording spirometry were done as per ATS recommendation that include; Checking the spirometer calibration, Explanation of the test to subject,

Preparation of the subject including asking about smoking, recent illness, medication use, etc. and measurement of weight and height without shoes. The subject were then instructed and demonstrated about the test including correct posture with head slightly elevated, rapid and complete inhalation and exhalation with maximal force.

After assuming the correct posture nose clip was attached and mouthpiece was placed in mouth with close lips around the mouthpiece. Patient was instructed to inhale completely and rapidly with a pause of one second at Total Lung Capacity and then to exhale maximally until no more air can be expelled while maintaining an upright posture. Repeated instructions were given. Minimum of three manoeuvres were repeated; no more than eight are usually required.

The variables recorded included FVC, FEV₁ and FEV₁ /FVC ratio. Three technically satisfactory measurements were obtained in which FVC was reproducible within 300 ml. The subject's FVC was defined as the maximal FVC which was determined before the DLCO test, as recommended by the ATS.

ATS RECOMMENDATION FOR PERFORMING DLCO⁵³

DLCO measurements were performed in compliance with the American Thoracic Society (ATS) guidelines. DLCO was measured using a single-breath technique. The DLCO was routinely adjusted for haemoglobin if the value was outside the normal range. Measurements of DLCO were made with a Collins automated system using a gas mixture that contained 0.3% Methane tracer gas and 0.3% carbon monoxide. The breath holding time was 10 seconds and the washout volume was 0.75 L. Each subject's height and weight were measured.

The participants were seated, wearing nose clips, and performed at least two DLCO manoeuvres separated by more than 4 minutes. The mean DLCO value from two manoeuvres that matched within 3 ml/min/mm Hg was reported.

Before the test was performed, each subject was instructed about all of the required manoeuvres. After the subject had adapted to the mouthpiece of the test apparatus, four or five tidal volumes were recorded to determine a regular end expiratory baseline. The subject was then asked to exhale as far as possible, to the point till maximal exhalation had been reached (residual volume RV); making a rapid, maximal inhalation within 2 to 2.5 seconds to VC continuing to hold the breath for 10 seconds while relaxing against a closed glottis and exhaling rapidly. If after two attempts an acceptable measurement could not be made, the procedure was then abandoned.

The values were interpreted as follows:

DLCO and DLCOHb : Normal(>80% predicted) Mild diffusion defect (65-80%), Moderate diffusion defect(45-65%) and severe diffusion defect(<45%).

FVC:Normal(>80% predicted), Mild Reduction(60-80%), Moderate Reduction(40-60%), Severe Reduction(<40%).

Statistical analysis

The following statistical analyses were performed to assess the strength of association between the variables of the study by using Chi-Square Test . HRCT pattern and DLCO in DPLD groups were compared by Mantel-Haenszel test for linear association and a p value of <0.05 was considered significant.

V. RESULTS

In our study 55 patients were screened for Diffuse Parenchymal Lung Diseases with collagen vascular diseases. Out of which 36 patients were taken up for the study after satisfying eligible criteria. All were nonsmokers. Remaining patients were excluded from the study group based on exclusion criteria.

AGE

In our study population age group ranges from 16-74 years.

Age Group (Years)	No of Patients	Percentage (%)
<35	9	25
36-45	11	30.56
46-55	7	19.44
>55	9	25
TOTAL	36	100

Maximum number of patients present presented between the ages of 36-45 years. The mean age distribution found in our study is 44. The calculated standard deviation is 13.79. Hence 95% of confidence interval lies in the range of 44 ± 4.5 , indicating that most of them fall in late fourth decade.

SEX

SEX	No of Patients	Percentage (%)
Male	12	33.33
Female	24	66.67
Total	36	100

The selected patients consisted of 66.67% Females and 33.33% males.

Male: Female sex ratio is 1:2 (Fig 2).

Disease classification

Disease	No of patients	Percentage (%)
Systemic Sclerosis	16	44.44
Rheumatoid Arthritis	12	33.33
Mixed Connective Tissue Disease	3	8.33
Systemic Lupus Erythematosus	2	5.56
Polymyositis/Dermatomyositis	2	5.56
Sjogren's syndrome	1	2.78
Total	36	100

Clinical Features

Clinical Features	No of Patients	
	Present(%)	Absent(%)
Exertional Dyspnoea	32(88.89%)	4(11.11%)
Cough	18(50%)	18(50%)
Chest pain	9(25%)	27(75%)
Bibasilar crackles	16(44.44)	20(55.56)

Rheumatoid arthritis and Systemic sclerosis form the bulk of the study population. Both constitute more than 75% of the cases. Followed by three cases of MCTD and two cases each from SLE and PM/DM and one case of Sjogren's syndrome. (Fig 3).

The predominant symptom found in majority of the study cases are Exertional dyspnoea(88.89%), followed by cough(50%) and chest pain(25%). Bibasilar crackles heard in 16(55.56%) cases out of 36 cases.

Extra pulmonary symptoms are Dyspepsia, Dyphagia, Raynaud's phenomenon, inflammatory arthritis, subcutaneous nodules, Sicca syndrome, Skin changes like rash, discolouration and thickening, proximal muscle weakness, etc . These above-mentioned symptoms present concomitantly in our cases and these symptoms have preceded or accompany with respiratory illness.

HRCT patterns

HRCT patterns	No of patients	Percentage (%)
RN	14	38.9
GGO	7	19.5
RGN	6	16.6
RGHT	5	13.9
RH	3	8.3
RGH	1	2.8
Total	36	100

R-Reticular,G-Ground glass ,H-Honey combing,T-Traction bronchiectasis, N-Nodular

In our study population various combinations of Reticular, Ground glass opacity, Honey combing, Traction bronchiectasis, and Nodular patterns were seen. Of which ReticuloNodular pattern forms the most common presentation(38.9%).Followed by Ground glass opacity(19.5%),RGN(16.6%)and RGHT(13.9%) . Less common being RH(8.3%) and RGN(2.8%) (Fig 4).

Individual patterns in HRCT

HRCT pattern	No of patients	Percentage (%)
Reticular	29	80.6
Nodular	21	58.3
Ground glass opacity	18	50
Honeycombing	8	22.2
Traction bronchiectasis	5	13.9

Reticular pattern is the most frequent presentation (80.6%) followed by Nodular pattern (58.3%) and GGO pattern(50%). Less common are Honeycombing and Traction bronchiectasis(22.2% and 13.9% respectively) (Fig 5).

Spirometry

Forced Vital capacity(FVC)	No patients	Percentage(%)
Normal	8	22.22
Mild restriction	6	16.67
Moderate restriction	18	50
Severe restriction	4	11.11
Total	36	100

Out of 36 cases of study population 28 cases were presented with restriction pattern (>75%) and remaining eight were presented with Normal FVC(22.22%). Forced vital capacity suggestive of Moderate restriction constitutes 50% of study population followed by Normal FVC(22.22%), Mild restriction(16.67%) and Severe restriction (11.11%) in decreasing frequency(Fig 6).

Diffusing capacity

Diffusing capacity	DLCO		DLCO Hb	
	No	(%)	No	(%)
Normal	5	13.89	5	13.89
Mildly reduced diffusing capacity	5	13.89	7	19.44
Moderately reduced diffusing capacity	7	19.44	6	16.67
Severely reduced diffusing capacity	19	52.78	18	50
Total	36	100	36	100

In DLCO Severely reduced diffusing capacity(52.78%) is the most common presentation in study population followed by moderately reduced diffusing capacity and then by equal presentations of Normal diffusing capacity and mildly reduced diffusing capacity(13.89% each).

In DLCO for corrected Haemoglobin Severely reduced diffusing capacity(50%) is the most common presentation in study population. Followed by mildly reduced diffusing capacity(19.44%), moderately reduced diffusing capacity(16.67%) and Normal diffusing capacity(13.89%). (Fig 7).

FVC Vs DLCO

FVC	Normal		Mild		Moderate		Severe		Total
	No	%	No	%	No	%	No	%	No
Normal	3	37.5	3	37.5	2	25	-	-	8
Mild	1	16.7	1	16.7	1	16.7	3	49.9	6
Moderate	1	5.6	1	5.6	4	22.1	12	66.7	18
Severe	-	-	-	-	-	-	4	100	4

FVC Vs DLCOHb

FVC	Normal		Mild		Moderate		Severe		Total
	No	%	No	%	No	%	No	%	No
Normal	3	37.5	5	62.5	-	-	-	-	8
Mild	1	16.7	1	16.7	1	16.7	3	49.9	6
Moderate	1	5.6	1	5.6	5	27.7	11	61.1	18
Severe	-	-	-	-	-	-	4	100	4

In both DLCO and DLCOHb Severly reducing diffusing capacity is associated with severe reduction in FVC in all 4 cases(100%). Out of five normal DLCO and DLCOHb patients two patients exhibit reduction in FVC (Fig 8).

HRCT Vs DLCO

HRCT patterns	Normal		Mild		Moderate		Severe		Total
	No	%	No	%	No	%	No	%	No
RN Reticulo Nodular	2	14.3	3	21.4	3	21.4	6	42.9	14
GGO Ground Glass Opacity	2	28.6	2	28.6	3	42.8	-	-	7
RNG Reticulo Nodular with Ground Glass Opacity	1	16.7	-	-	1	16.7	4	66.6	6
RGHT Reticular, Ground glass opacity, Honeycombing &Traction bronchiectasis	-	-	-	-	-	-	5	100	5
RH Reticular & Honeycombing	-	-	-	-	-	-	3	100	3
RGH Reticular, Ground glass opacity& Honeycombing	-	-	-	-	-	-	1	100	1

The various presentations of HRCT patterns in each individual were correlated with Diffusing capacity(DLCO). Out of 14 cases of RN(ReticuloNodular) pattern 6 cases(42.9%) were present in severely reduced diffusing capacity followed by 3 cases(21.4%) each in mild and moderately reduced diffusing capacity, then 2 cases(14.3%) in normal diffusing capacity.

Out of 7 cases of GGO(Ground Glass Opacity) 3 cases(42.8%) were present in moderately reduced diffusing capacity followed by 2 cases(28.6%) each in normal and mildly reduced diffusing capacity.

Out of 6 cases of RGN (Reticular, Ground glass opacity, Nodular) pattern 4 cases(66.6%) were present in severely reduced diffusing capacity followed by one case (16.7%) each in Normal diffusing capacity and moderately reduced diffusing capacity.

All 5 cases(100%) of RGHT (Reticular, Ground glass opacity, Honeycombing and Traction bronchiectasis) pattern present only in severely reduced diffusing capacity.

Out of 3 cases of RH (Reticular, Honeycombing) pattern all (100%) were present in severely reduced diffusing capacity.

1 case(100%) of RGH (Reticular, Ground glass opacity, Honeycombing) pattern was present in severely reduced diffusing capacity (Fig9).

HRCT Vs DLCOHb

HRCT patterns	Normal		Mild		Moderate		Severe		Total
	No	%	No	%	No	%	No	%	No
RN Reticulo Nodular	2	14.3	3	21.4	3	21.4	6	42.9	14
GGO Ground Glass Opacity	2	28.6	4	57.1	1	16.7	-	-	7
RNG Reticulo Nodular with Ground Glass Opacity	1	16.7	-	-	1	16.7	4	66.6	6
RGHT Reticular, Ground glass opacity, Honeycombing &Traction bronchiectasis	-	-	-	-	-	-	5	100	5
RH Reticular & Honeycombing	-	-	-	-	1	33.3	2	66.7	3
RGH Reticular, Ground glass opacity& Honeycombing	-	-	-	-	-	-	1	100	1

The various presentations of HRCT pattern in each individual is correlated with Diffusing capacity for corrected Haemoglobin(DLCOHb).

Out of 14 cases of RN(ReticuloNodular) pattern 6 cases(42.9%) were present in severely reduced diffusing capacity followed by 3 cases(21.4%) each in Mild and moderately reduced diffusing capacity, then 2 cases(14.3%) in Normal diffusing capacity.

Out of 7 cases of GGO(Ground Glass Opacity) 4 cases(57.1%) were present in mildly reduced diffusing capacity followed by 2 cases(28.6%) in Normal and 1 case (14.3%) in moderately reduced diffusing capacity.

Out of 6 cases of RGN (Reticular, Ground glass opacity, Nodular) pattern 4 cases(66.6%) were present in severely reduced diffusing capacity followed by one case (16.7%) each in Normal diffusing capacity and moderately reduced diffusing capacity.

All 5 cases(100%) of RGHT (Reticular, Ground glass opacity, Honeycombing and Traction bronchiectasis) pattern present only in severely reduced diffusing capacity.

Out of 3 cases of RH (Reticular, Honeycombing) pattern 2 cases (66.7%) were present in severely reduced diffusing capacity followed by 1 case in(33.3%) moderately reduced diffusing capacity .

1 case(100%) of RGH (Reticular, Ground glass opacity, Honeycombing) pattern was present in severely reduced diffusing capacity (Fig10).

INDIVIDUAL HRCT PATTERN Vs DLCO

Individual HRCT pattern	Normal		Mild		Moderate		Severe		Total
	No	%	No	%	No	%	No	%	
Reticular	3	10.3	3	10.3	4	13.8	19	65.6	29
Nodular	3	14.3	3	14.3	4	19	11	52.4	21
GGO	3	16.7	2	11.1	3	16.7	10	55.6	18
Honeycombing	-	-	-	-	-	-	8	100	8
Traction Bronchiectasis	-	-	-	-	-	-	5	100	5

Out of 29 cases of Reticular pattern 19 cases(65.6%) were present in Severely reduced diffusing capacity followed by 4 cases(13.8%) in moderately reduced diffusing capacity and 3 cases(10.3%) each in normal diffusing capacity and mildly reduced diffusing capacity.

Out of 21 cases of Nodular pattern 11 cases(52.4%) were present in Severely reduced diffusing capacity followed by 4 cases(19%) in moderately reduced diffusing capacity and 3 cases(14.3%) each in normal diffusing capacity and mildly reduced diffusing capacity.

Out of 18 cases of GGO pattern 10 cases(55.6%) were present in Severely reduced diffusing capacity followed by 3 cases(16.7%) each in moderately reduced

diffusing capacity and normal diffusing capacity and 2 cases(11.1%) in mildly reduced diffusing capacity.

All 8 cases(100%) of Honeycombing pattern 19 cases were present in Severely reduced diffusing capacity.

All 5 cases(100%) of Traction Bronchiectasis pattern were present in Severely reduced diffusing capacity (Fig 11).

INDIVIDUAL HRCT PATTERN Vs DLCOHb

Individual HRCT pattern	Normal		Mild		Moderate		Severe		Total
	No	%	No	%	No	%	No	%	
Reticular	3	10.3	3	10.3	5	17.2	18	62.2	29
Nodular	3	14.3	3	14.3	4	19	11	52.4	21
GGO	3	16.7	3	16.7	2	11.1	10	55.6	18
Honeycombing	-	-	-	-	1	12.5	7	87.5	8
Traction Bronchiectasis	-	-	-	-	-	-	5	100	5

Out of 29 cases of Reticular pattern 18 cases(62.2%) were present in Severely reduced diffusing capacity followed by 5 cases(17.2%) in moderately reduced diffusing

capacity and 3 cases(10.3%) each in normal diffusing capacity and mildly reduced diffusing capacity.

Out of 21 cases of Nodular pattern 11 cases(52.4%) were present in Severely reduced diffusing capacity followed by 4 cases(19%) in moderately reduced diffusing capacity and 3 cases(14.3%) each in normal diffusing capacity and mildly reduced diffusing capacity.

Out of 18 cases of GGO pattern 10 cases(55.6%) were present in Severely reduced diffusing capacity followed by 3 cases(16.7%) each in mildly reduced diffusing capacity and normal diffusing capacity and 2 cases(11.1%) in moderately reduced diffusing capacity.

Out of 8 cases of Honeycombing pattern 7 cases(87.5%) were present in Severely reduced diffusing capacity and one case(12.5%) in moderately reduced diffusing capacity.

All 5 cases(100%) of Traction Bronchiectasis pattern were present in Severely reduced diffusing capacity (Fig 11).

Significant p value association occurs between the HRCT patterns and DLCOHb at 5% level by using Chi- Square Mantel-Haenszel test for linear association.

Significant p value association occurs between the HRCT patterns and FVC at 1% level by using Chi- Square Mantel-Haenszel test for linear association.

Significant p value association occurs between FVC Vs DLCO(p value 0 .0001) also FVC Vs DLCO Hb (p value 0.003) at 1% level by using Chi-Square Mantel Haenszel test for linear association.

Reticular Pattern was the most frequent presentation (80.6%), and has significant p value association with DLCO & DLCO Hb by using Chi-Square Pearson test for linear association.

Significant p value association occurs between the Honeycombing pattern and DLCO and DLCOHb by using Chi- Square Pearson test for linear association.

VI. DISCUSSION

Our study principally focuses on characterisation of HRCT pattern of DPLD analysed by comparing with Spirometry (Forced Vital Capacity) and Diffusing capacity for Carbon monoxide(DLCO) and for Diffusing capacity of Carbon monoxide for corrected Haemoglobin(DLCOHb).

In our study group most of them fell in late fourth decade. Female predominance is noted in DPLD with collagen vascular disease patients.

Rheumatoid arthritis and Systemic sclerosis constitute more than 75% of the cases. All cases with FVC presented as either restriction or Normal FVC. FVC presented with restriction pattern in >75% of study population. The predominant symptom found in majority of the study cases are Exertional dyspnoea pattern (16.67%)

In HRCT pattern ReticuloNodular pattern forms the most common presentation (38.9%) followed by GGO(16.67%).

When individual HRCT patterns concerned Reticular Pattern was the most frequent presentation (80.6%), and had significant association of p value 0.007 with severely reducing diffusing capacity(DLCO Hb).

All patients with RGHT and RGH patterns had severe reduction in DLCO. Severe reduction in DLCO was also found in two thirds of patients with RH and RNG, less than half of patients with RN and was rare in patients with GGO.

In WELLS et al.²⁰ study, DLCO is the best index of the extent of the DPLD when compared with HRCT as the "gold standard".

Warrick et al⁵⁴ has defined a score based on the criteria of type and extent of HRCT signs in systemic sclerosis patients. They found a negative correlation between single-breath carbon monoxide lung diffusion capacity (DLCO) and HRCT score. But later Diot et al⁵⁵ found a strong inverse correlation between HRCT score and DLCO ($p < 0.0002$) in SS patients.

We were able to confirm the correlation observed between DLCO and DLCOHb and certain HRCT patterns in DPLD with collagen vascular disease patients.

In Demosthenes Bouros, Athol U. Wells et al⁵⁷ study in PSS Outcome is linked more strongly to disease severity at presentation and serial DLCO trends than to histopathologic findings. The percent predicted DLCO best reflects the extent of fibrosing alveolitis in PSS, and therefore should be measured in routine evaluations⁵².

In Bodolay et al⁵⁶ study of MCTD population, reduced DLCO was the most sensitive test for predicting the presence of fibrosing alveolitis on HRCT, but the overall correlation of pulmonary function with radiographic appearance was poor.

5 cases of Normal DLCO Hb are associated with 2 cases each of Reticulonodular pattern and GGO pattern and 1 case with RGN(Reticular, Ground glass opacity, Nodular) pattern (significant p value < 0.05). Out of five normal DLCO and DLCOHb patients two patients exhibit reduction in FVC. This is probably explained by correlation with age(both are above 60 years).

All HRCT patterns have reduced FVC but significant reduction with RGHT pattern.

VII. CONCLUSION

Altered DLCO may be the first and only abnormality found in early stage of Diffuse parenchymal lung diseases. The earlier discussed studies show the correlation between individual collagen vascular disease and pulmonary function testing. But this study focuses on evaluation of Diffusing capacity for carbon monoxide among patients with Diffuse parenchymal lung diseases in all classified Collagen vascular diseases showing various HRCT pattern abnormalities and correlate the same with spirometry.

Among the various combinations of HRCT patterns in Collagen vascular diseases presence of Honeycombing is associated with significant severe reduction in DLCO and DLCOHb with varying grades of severity in Forced vital capacity. When individual HRCT patterns analysed Honeycombing and Traction bronchiectasis patterns have significant severe reduction in DLCO and DLCOHb with varying grades of spirometry severity.

When DLCO and DLCOHb are within normal limits the reduction in Forced vital capacity has to be correlated with age factor.

In summary DLCO and DLCOHb are in significant association with spirometry. The percent predicted DLCO and DLCOHb best reflect the extent of Honeycombing which is considered as fibrotic index in Diffuse parenchymal lung diseases with Collagen vascular diseases, and therefore should be measured in routine evaluations.

So we conclude DLCO and DLCOHb in collagen vascular disease will be of use in initial evaluation of severity of collagen vascular disease as well as to assess the response to treatment in these disorders.

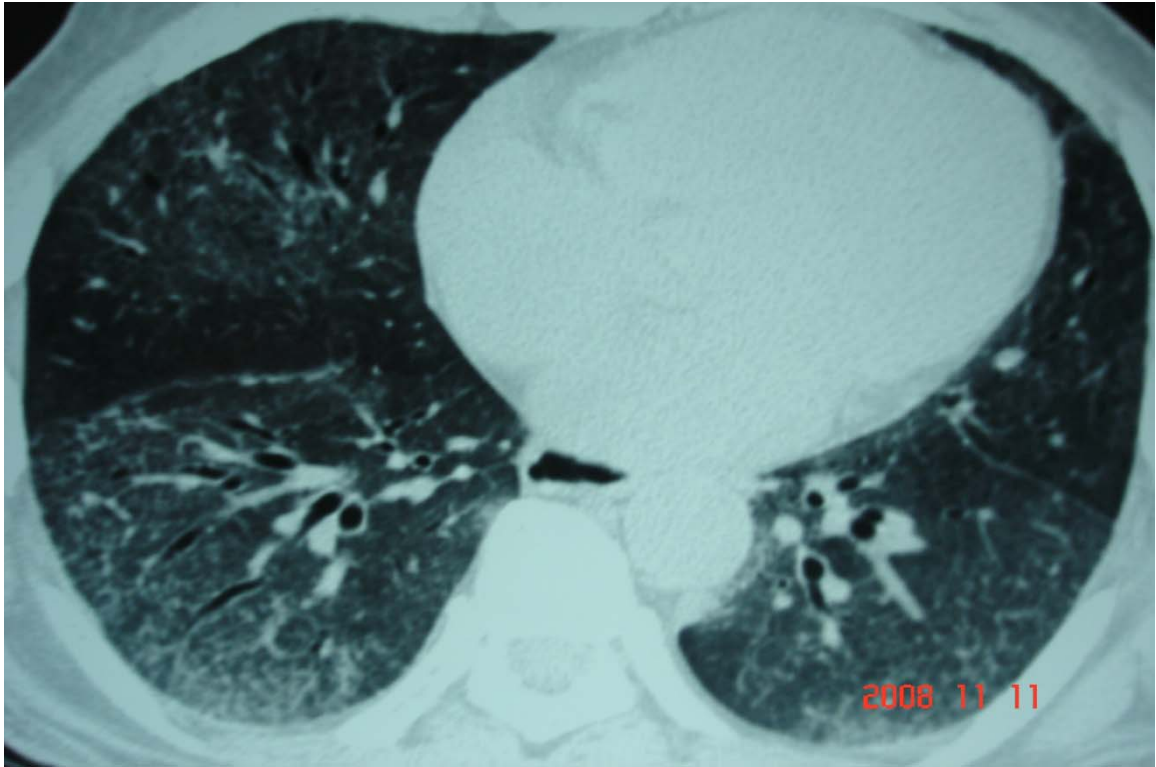


Fig:A Ground Glass Opacity &Traction Bronchiectasis



Fig:B Bilateral Reticular opacities



Fig:C Reticulonodular with Honeycombing

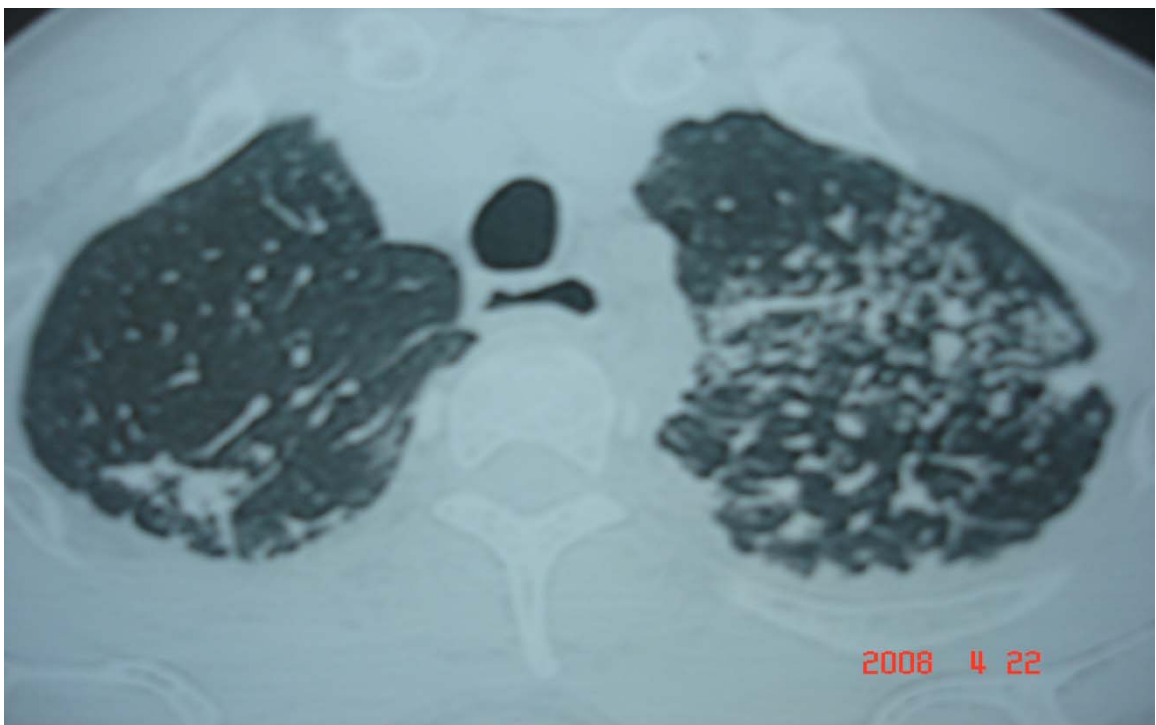


Fig:D Reticulonodular with Dilated Esophagus

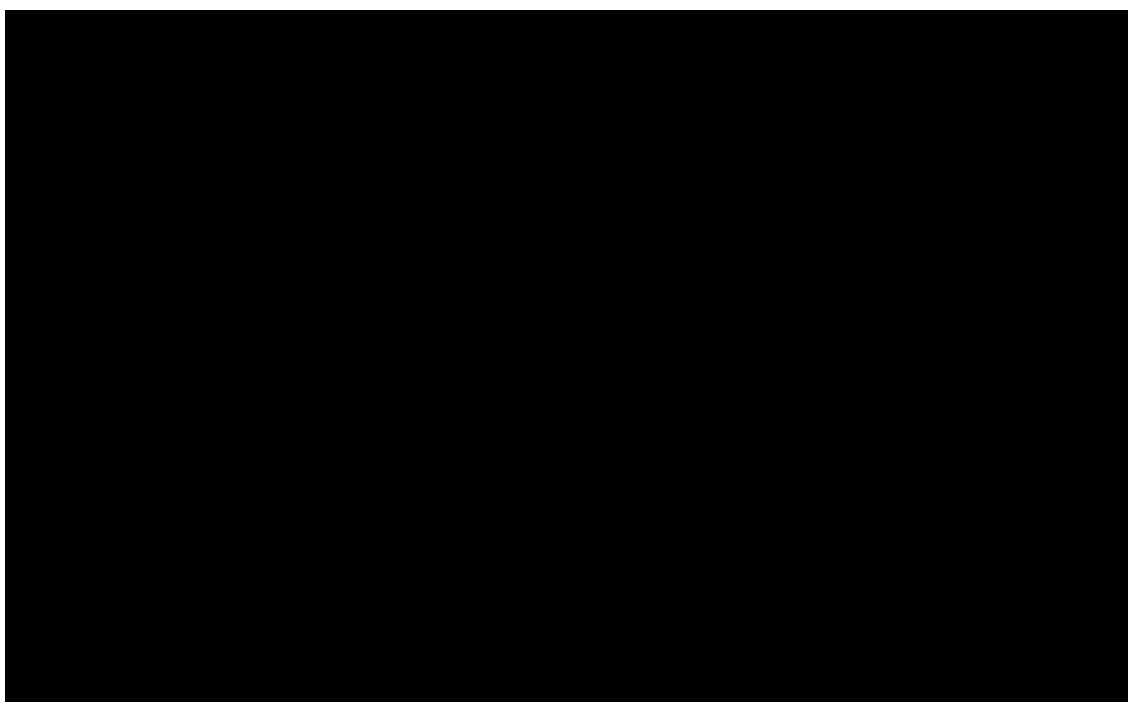


Fig 1. Age group

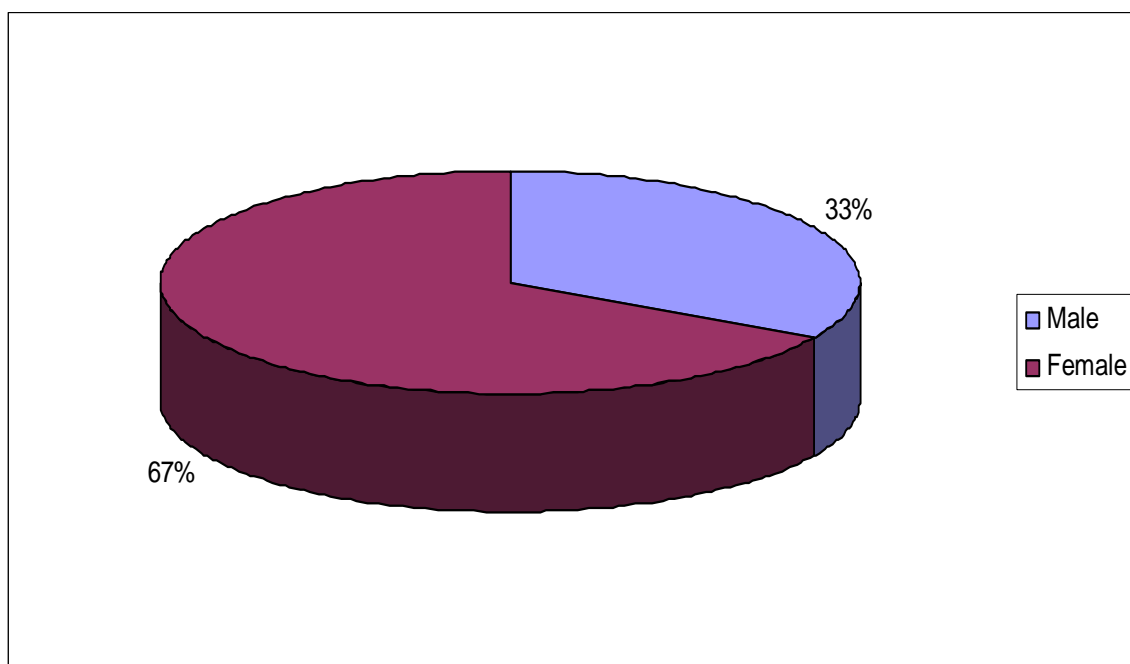
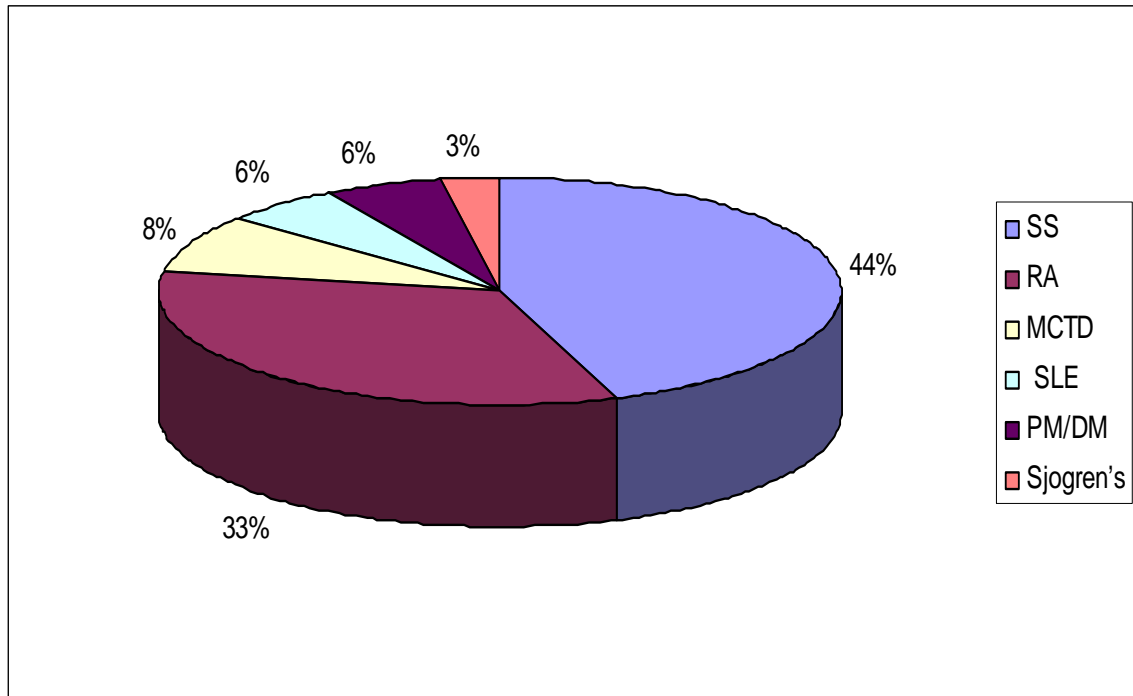
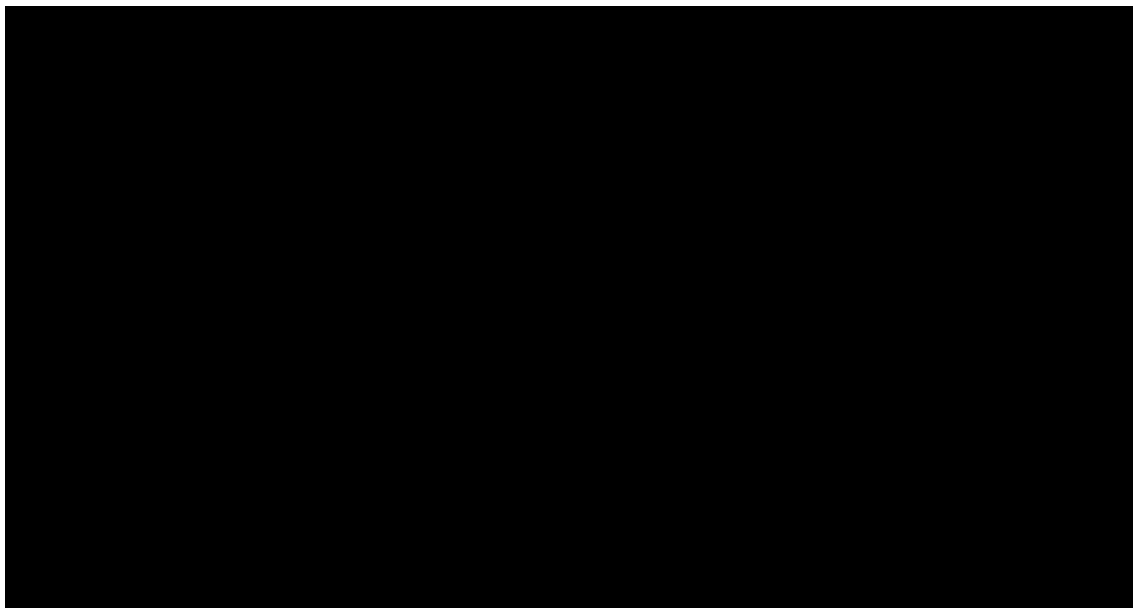


Fig 2. Sex



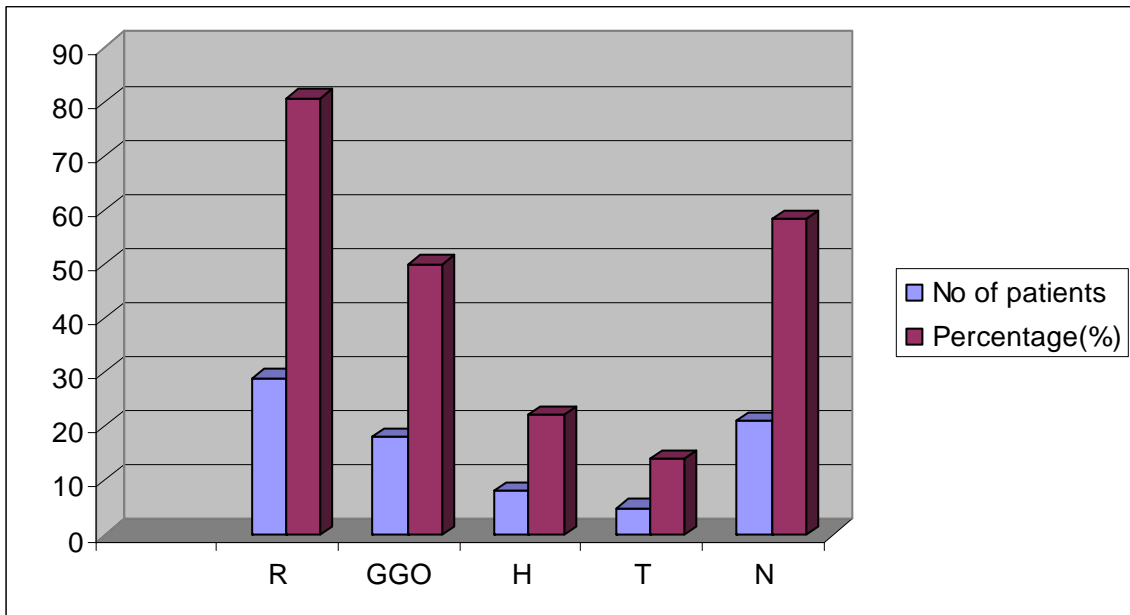
SS-Systemic Sclerosis, RA-Rheumatoid Arthritis, MCTD-Mixed Connective Tissue Disease, SLE-Systemic Lupus Erythematosus, PM/DM-Polymyositis/Dermatomyositis, Sjogren's-Sjogren's syndrome

Fig 3. Disease classification



RN-Reticulo Nodular, GGO-Ground Glass Opacity, RNG- Reticulo Nodular with Ground Glass Opacity , RGHT- Reticular, Ground glass opacity, Honeycombing & Traction bronchiectasis, RH-Reticular & Honeycombing, RGH-Reticular, Ground glass opacity& Honeycombing

Fig 4. HRCT Patterns



R-Reticular,GGO-Ground glass Opacity ,H-Honey combing,T-Traction bronchiectasis, N-Nodular

Fig 5. HRCT Individual patterns

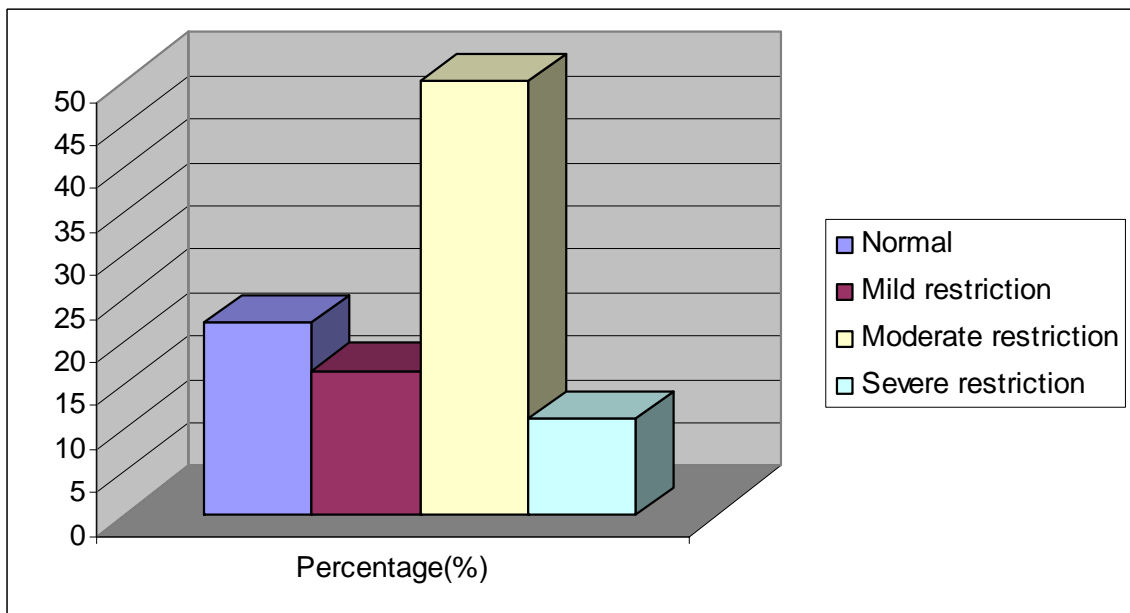
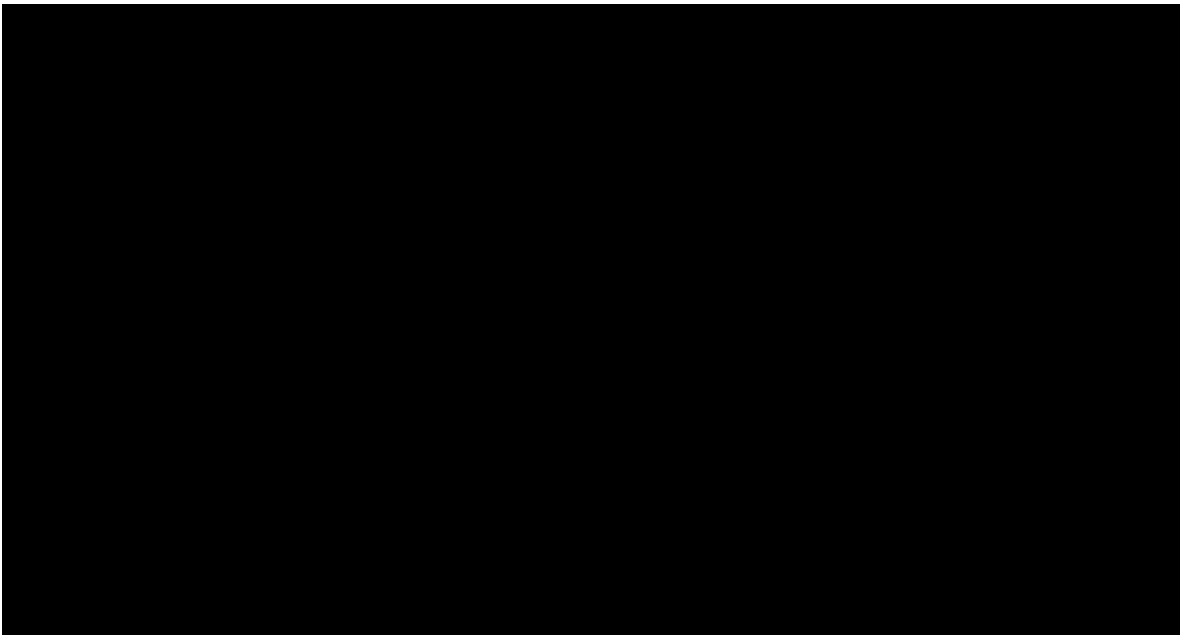
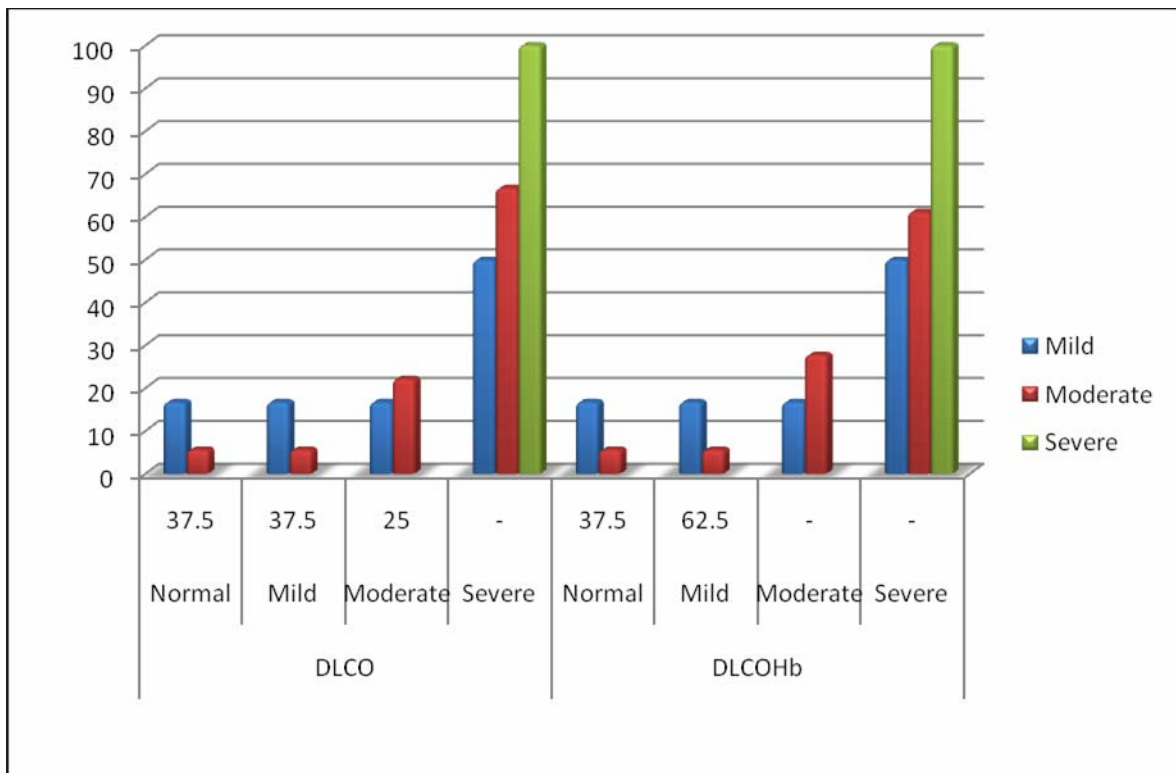


Fig 6. FVC



Mild-Mildly reduced diffusing capacity, Moderate-Moderately reduced diffusing capacity, Severe-Severely reduced diffusing capacity

Fig 7. Diffusing capacity



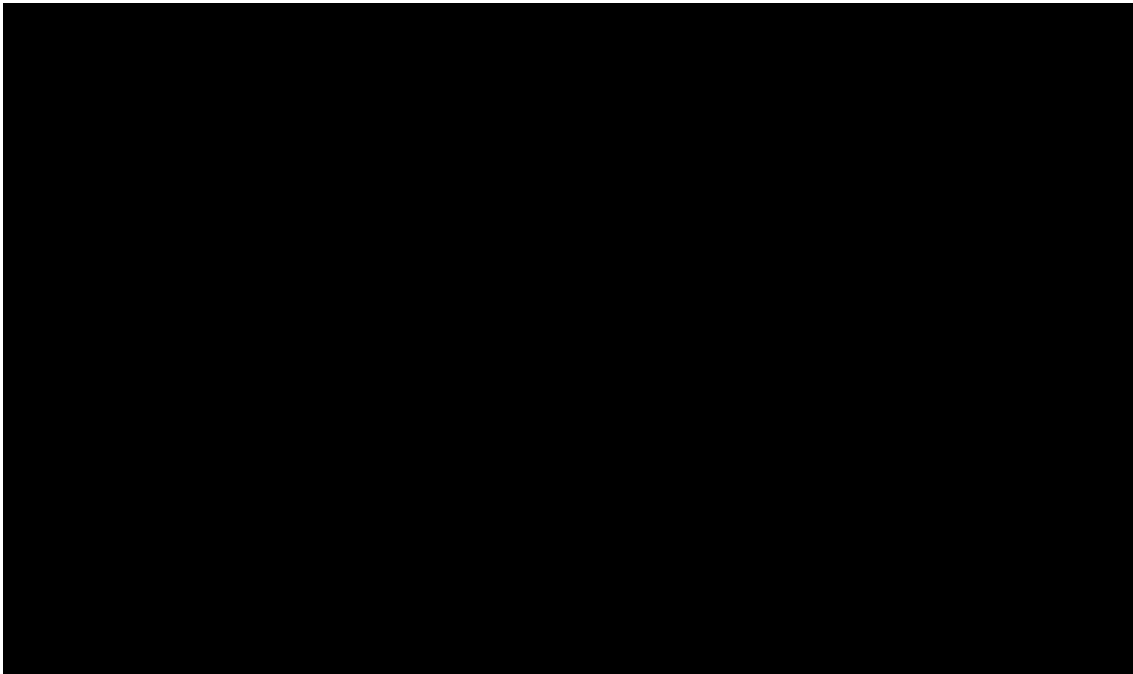
Mild-Mildly reduced diffusing capacity, Moderate-Moderately reduced diffusing capacity, Severe-Severely reduced diffusing capacity

Fig.8 FVC VS DLCO&DLCOHb



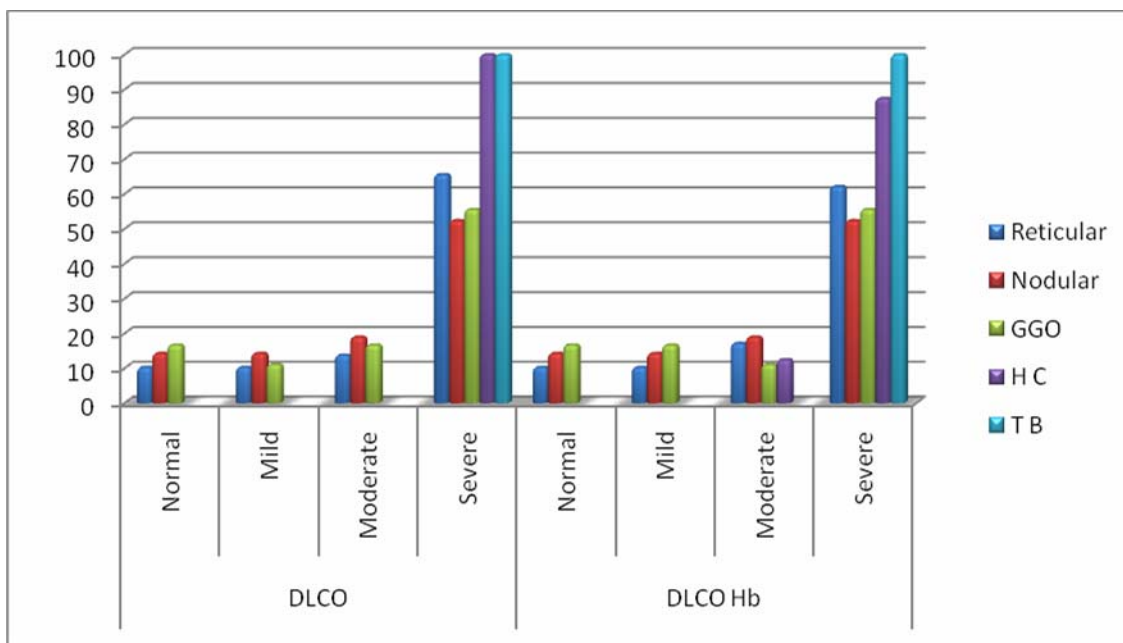
RN-Reticulo Nodular, GGO-Ground Glass Opacity, RNG- Reticulo Nodular with Ground Glass Opacity , RGHT- Reticular, Ground glass opacity, Honeycombing & Traction bronchiectasis, RH-Reticular & Honeycombing, RGH-Reticular, Ground glass opacity& Honeycombing

Fig 9. HRCT Vs DLCO



RN-Reticulo Nodular, GGO-Ground Glass Opacity, RNG- Reticulo Nodular with Ground Glass Opacity , RGHT- Reticular, Ground glass opacity, Honeycombing & Traction bronchiectasis, RH-Reticular & Honeycombing, RGH-Reticular, Ground glass opacity& Honeycombing

Fig 10. HRCT Vs DLCOHb



GGO-Ground Glass Opacity, HC- Honey combing, TB-Traction Bronchiectasis

Fig 11. INDIVIDUAL HRCT PATTERN Vs DLCO&DLCOHb



FIG 12. COLLINS AUTOMATED SYSTEM FOR PERFORMING DLCO

VIII. ABBREVIATION

ATS	American Thoracic Society
CVD	Collagen Vascular Disease
DIP	Diffuse Interstitial Pneumonia
DLCO	Diffusing Capacity for Carbon Monoxide
DLCO/VA	Diffusing capacity for carbon monoxide per unit of alveolar volume
DPLD	Diffuse Parenchymal Lung Disease
FEV1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GGO	Ground Glass Opacity
Hb	Haemoglobin
HRCT	High Resolution Computerised Tomography
ILD	Interstitial lung diseases
KCO	Transfer coefficient of the lung (DLCO/VA)
LIP	Lymphocytic Interstitial Pneumonitis
MCTD	Mixed Connective Tissue Disease
NSIP	Non-Specific Interstitial Pneumonitis
PFT	Pulmonary Function Test
PM/DM	Polymyositis/Dermatomyositis
RA	Rheumatoid Arthritis
RBILD	Respiratory Bronchiolitis Interstitial Lung Disease
SLE	Systemic Lupus Erythematosus
SS	Systemic Sclerosis
UIP	Usual interstitial pneumonia
VA	Alveolar Volume
VD	Dead space volume

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X. MASTER CHART

SNO	ID	NAME	AGE	Sex	Diagnosis	FVC	Restriction	DLCO	Reported	DLCOHb	Reported	HRCT
1	21146	Dhanamal	68	F	SS	76	Mild	22	Severe	23	Severe	RGHT
2	16922	Saroja	60	F	SS	51	Moderate	22	Severe	23	Severe	RN
3	24742	Annamalai	56	M	SS	62	Moderate	32	Severe	32	Severe	RGH
4	20320	Perumal	48	M	SS	90	Normal	63	Moderate	69	Mild	GGO
5	15165	Desingh	46	M	SS	50	Moderate	59	Moderate	64	Moderate	RN
6	19434	Lalitha	53	F	SS	67	Mild	25	Severe	27	Severe	RGN
7	21699	Ranjitha	16	F	SS	60	Moderate	42	Severe	50	Moderate	RH
8	50167	Selvi	37	F	SS	33	Severe	15	Severe	16	Severe	RGHT
9	23083	Alli	42	F	SS	45	Moderate	26	Severe	30	Severe	RN
10	24127	Chellamma	40	F	SS	95	Normal	81	Normal	88	Normal	RN
11	23874	Devaki	45	F	SS	80	Normal	69	Mild	74	Mild	GGO
12	24609	Devi	45	F	SS	52	Moderate	23	Severe	25	Severe	RGHT
13	20788	Rajeswari	32	F	SS	85	Normal	61	Moderate	66	Mild	GGO
14	17631	Venkatesan	50	M	SS	54	Moderate	57	Moderate	59	Moderate	RN
15	21876	Chinnamal	30	F	SS	50	Moderate	39	Severe	40	Severe	RH
16	23775	Anusya	31	F	SS	70	Mild	73	Mild	79	Mild	GGO
17	21607	Kanniappan	33	M	RA	87	Normal	90	Normal	111	Normal	RN
18	9626	Dhillaiammal	50	F	RA	56	Moderate	58	Moderate	63	Moderate	RGN
19	16325	Pankajam	63	F	RA	47	Moderate	108	Normal	123	Normal	RGN
20	48044	Pakirisamy	62	M	RA	21	Severe	38	Severe	38	Severe	RGHT
21	22044	Prakasam	65	M	RA	74	Mild	107	Normal	114	Normal	GGO
22	22192	Gopal	58	M	RA	44	Moderate	23	Severe	28	Severe	RN
23	21774	Varadhan	56	M	RA	84	Normal	67	Mild	72	Mild	RN
24	16872	Sundari	74	F	RA	62	Moderate	24	Severe	26	Severe	RN
25	22096	Dhanalakshmi	48	F	RA	64	Moderate	37	Severe	36	Severe	RN
26	22234	Dhanapackiam	40	F	RA	89	Normal	83	Normal	85	Normal	GGO
27	67507	Murugaiyan	43	M	RA	65	Mild	58	Moderate	58	Moderate	RN
28	15890	Selvakumar	40	M	RA	77	Mild	22	Severe	25	Severe	RN
29	50229	Shakeela	30	F	SLE	42	Moderate	24	Severe	28	Severe	RGN
30	13175	Vasantha	48	F	SLE	44	Moderate	29	Severe	30	Severe	RN
31	49759	Kala	42	F	PM/DM	53	Moderate	29	Severe	30	Severe	RGN
32	9449	Jeyapaul	21	M	PM/DM	52	Moderate	59	Moderate	60	Moderate	GGO
33	23128	Aruna sundar	38	F	MCTD	88	Normal	66	Mild	75	Mild	RN
34	16888	Menaka	23	F	MCTD	27	Severe	11	Severe	11	Severe	RGN
35	23163	Gunaselvi	26	F	MCTD	34	Severe	11	Severe	12	Severe	RGHT
36	22099	Kannika	36	F	Sjogrens	50	Moderate	63	Mild	66	Mild	RN

XI. KEY TO THE MASTER CHART

SEX

M - Male

F - Female

DIGNOSIS

SS - Systemic sclerosis

RA - Rheumatoid arthritis

SLE - Systemic lupus Erythematosus

PM/DM - Polymyositis/Dermatomyositis

MCTD - Mixed connective tissue disease

FVC REPORTED

Normal - Normal FVC

Mild - Mild restriction

Moderate - Moderate restriction

Severe - Severe restriction

DLCO&DLCOHb REPORTED

Normal - Normal DLCO &DLCOHb

Mild - Mildly reduced diffusing capacity

Moderate - Moderately reduced diffusing capacity

Severe - Severely reduced diffusing capacity

HRCT PATTERNS

RN - Reticulo Nodular

GGO - Ground Glass Opacity

RNG - Reticulo Nodular with Ground Glass Opacity

RGHT - Reticular, Ground glass opacity, Honeycombing & Traction
bronchiectasis

RH - Reticular & Honeycombing

RGH - Reticular, Ground glass opacity& Honeycombing

INSTITUTIONAL ETHICAL COMMITTEE
GOVERNMENT GENERAL HOSPITAL & MADRAS MEDICAL COLLEGE
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K.Dis.No.16328 P & D3/Ethics/Dean/GGH/08

Dated: 8.9.2008

Title of the work

: "patients of diffuse parenchymal lung disease Manifestations in collagen vascular disease and in relation to d/co"

Principal Investigator

: Dr. G. Sangamithra

Department

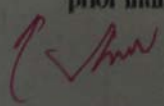
: TB & chest diseases. MMC, Ch.3.

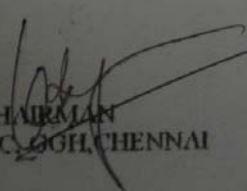
The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 10th September 2008 at 2 P.M in Government General Hospital, Deans, Chamber, Chennai-3.

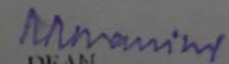
The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The principal investigator and their team are directed to adhere the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of any change of study procedure, site and investigation or guide.
4. You should not deviate from the area of the work for which I applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulations of the institution(s).
7. You should complete the work within the specific period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.


SECRETARY
IEC, GGH, CHENNAI


CHAIRMAN
IEC, GGH, CHENNAI


DEAN
GGH & MMC, CHENNAI

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